The Third Memorial Workshop for Kazuhide Mori on Computational Sciences

Discretized Curvature Analysis for Ribose and Adenine Rings of ATP–Analogs Bound to Myosin

Yoshinori Nagai[1], Kei Yura[2], Hiroshi Kagawa[3], and Hiroshi Wako[4]

1. Introduction

We are investigating structural changes of myosin molecules by ATP hydrolysis in atomic level, and also studying molecular orbital of the partly selected amino acid residues and ATP–analog found in crystallographic data of ATP–analogs bound to myosin molecules. The crystallographic data are obtained from PDB. We calculated the curvatures of rings in ATP, namely ribose and adenine. The curvature calculation was found to be in discretized manner. We compared the discretized curvatures of ribose and adenine of ATP–analogs bound to myosin molecules with those bound to ATP–binding proteins that release a phosphate when they hydrolyze ATP. The function of ATP–binding proteins was classified based on the chemical structure of the product. The classified categories include Pi release protein, Pi transfer protein, PPi release protein and no hydrolysis protein, and myosin belongs to the group of Pi release proteins. We discuss structure of ATP–analogs by comparison the ring curvatures of ATP–analogs with those of ATP found in PDB. Sections 2 and 3 are devoted to the explanation of the types of discretized curvatures we calculated. Section 4 describes the geometrical relationship among rings and Section 5 is the summary.

2. Procedure for curvature analysis of ATP rings

In this study, we characterized the discrete ring curvatures on the gravity center as shown in Fig. 1 where we draw the ring structure in the case of pentagon.

The quantities used in this study were curvatures of rings in a discrete sense. We adopted the method to calculate curvatures from S. Hyde (J. Chem. Phys. 93 (1989) 1464–1471). The calculated discretized curvatures were Gaussian curvature (K) and mean curvature (H) given by following equations.

$$\text{Gaussian curvature: } K = \frac{3\left(2\pi - \sum_{(i,j)} \theta_{ij}\right)}{\sum_{(i,j)} A_{ij}}, \quad \text{Mean curvature: } H = \frac{3\sum_{i}(\pi - \delta_i)}{\sum_{(i,j)} A_{ij}}$$

In the expression above, A_{ij} is the area of triangle spanned by atoms i, j, and the gravity cen-

[1] Center for Information Science, Kokushikan University, Tokyo, Japan
[2] Computational Biology, Graduate School of Humanities and Sciences, Ochanomizu University, Tokyo, Japan
[3] Physics Laboratory, Nippon Medical School, Kawasaki, Japan
[4] School of Social Sciences, Waseda University, Tokyo, Japan

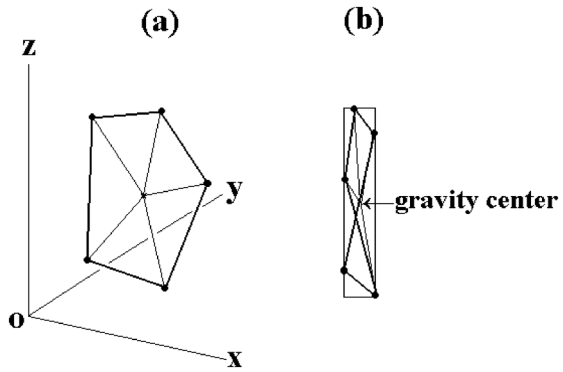


Fig. 1 Location of a pentagon (a), and its side view (b)

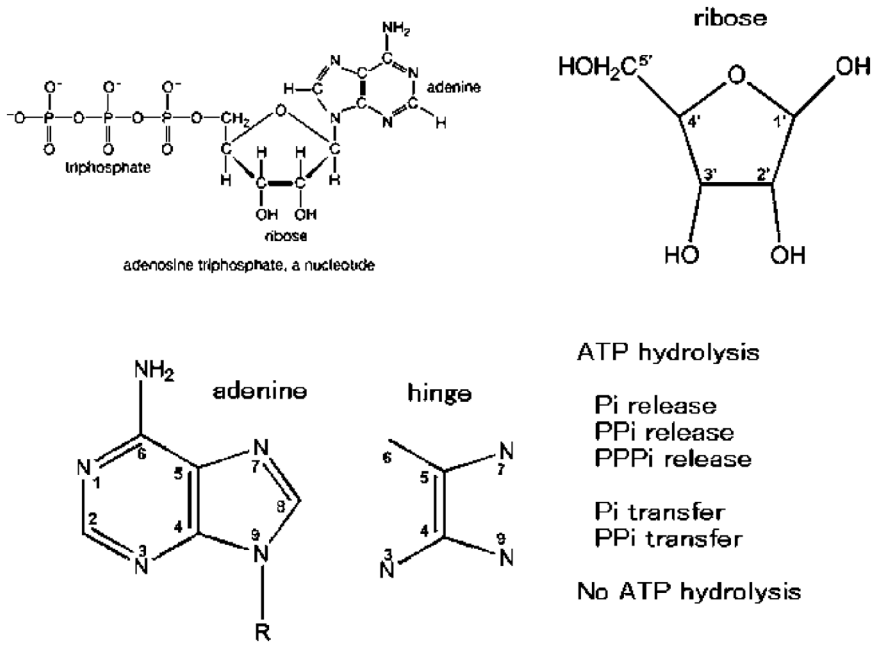


Fig. 2 ATP structure, numbering of atoms of ribose and adenine, and the classification of ATP function by phosphate hydrolysis events

ter. θ_{ij}, is the angle between two lines, namely the line drawn between atom i and the gravity center and that between atom j and the gravity center. δ_i is the dihedral angle between two triangles over the line drawn between atom i and the gravity center. As shown in Fig. 1, the Gaussian curvature for the gravity center always has a negative value.

ATP molecule has three types of rings, i.e., a pentagon of ribose, and a hexagon and a pentagon of adenine as shown in Fig. 2. The numbering of atoms of ATP rings is also described in Fig. 2. The curvatures of these three rings of ATP are demonstrated in Section 3. In order to describe the flatness of adenine, namely, the relative orientation between five- and six-member rings, we calculated the curvatures for the hinge part of the adenine as defined in Fig. 2. We also calculated the

curvatures of connecting part between adenine and ribose rings to know mutual disposition between adenine and ribose. Actual calculation was performed over the following atoms with the analogy to the adenine hinge part; (C_4, C_8)–N_9–C_1'–(O_1', C_2').

3. Curvatures of ribose and adenine

Ribose curvatures are shown in Fig. 3 (A) and (B). Fig. 4 (A) and (B) denote the Gaussian and the mean curvatures of adenine five-membered rings. Fig. 5 (A) and (B) show the curvatures of adenine six-membered rings.

The five-membered ring of the adenine bound to Pi release proteins is flat as seen in Fig. 4 (A). The five-membered ring of the adenine of ATP–analog bound to myosin is, however, less flat than that of ATP bound to Pi release protein. In the figure, the curvatures of the rings of ATP–analog are generally located on around outside of the curvature distribution obtained from ATP bound to Pi release proteins. It is difficult to find any correlations among Fig. 3(B), Fig. 4(B), and Fig. 5(B).

4. Relationship between the rings of adenine and the surface relationship between adenine and ribose.

In order to understand the dynamics of adenine structure, we investigated the relationship between five- and six-membered rings of adenine. For this purpose, we calculated the curvature of the adenine hinge, which consists of atoms N_3, C_4, N_9, N_5, C_5, and C_6. The order of atoms for curvature calculation was either clockwise or counterclockwise and is in the manner to draw unicursal

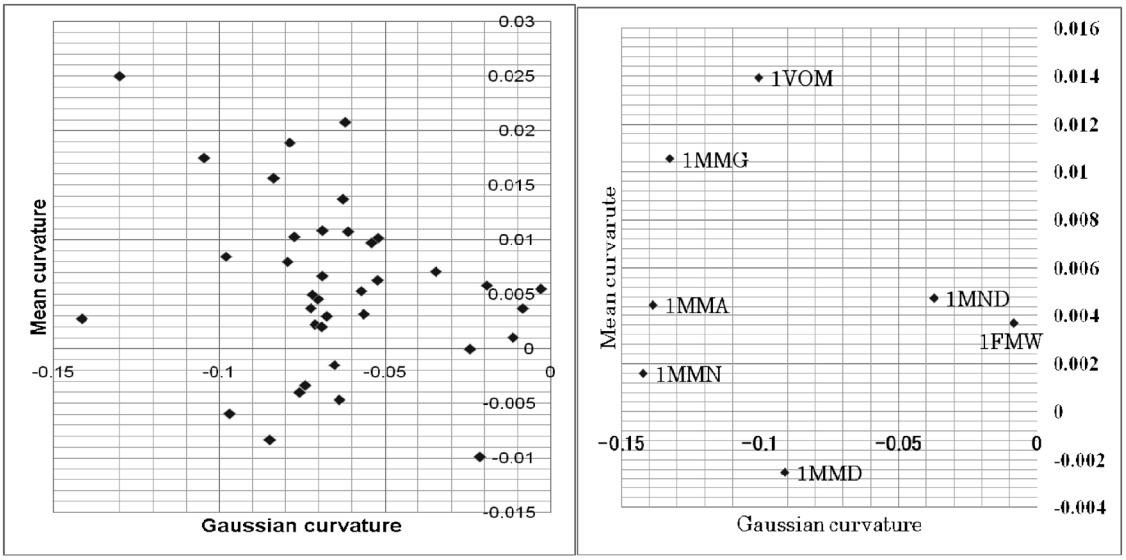
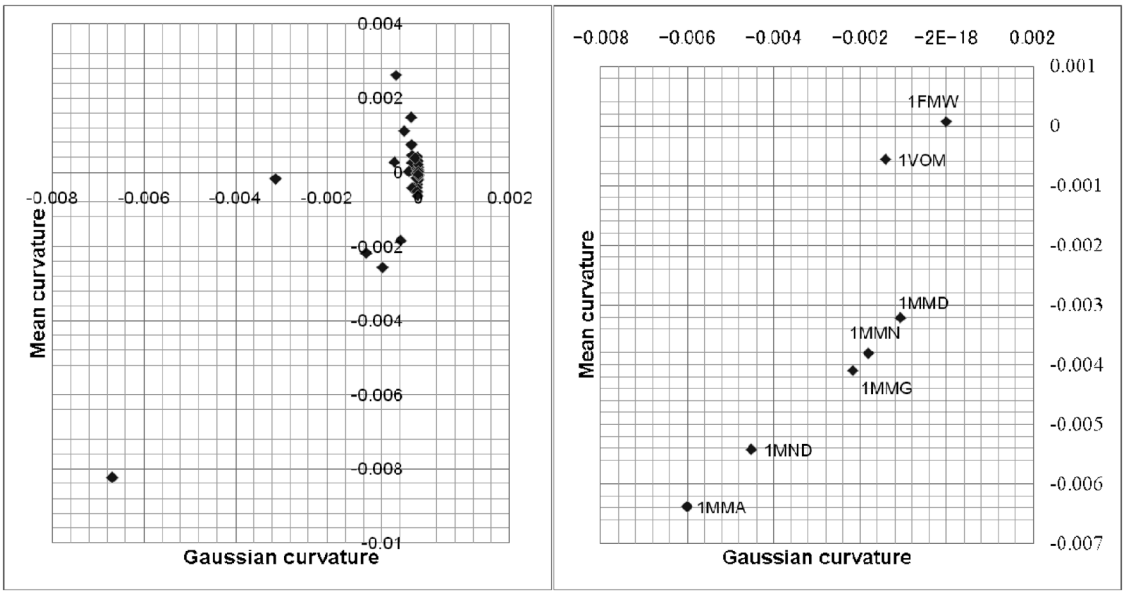
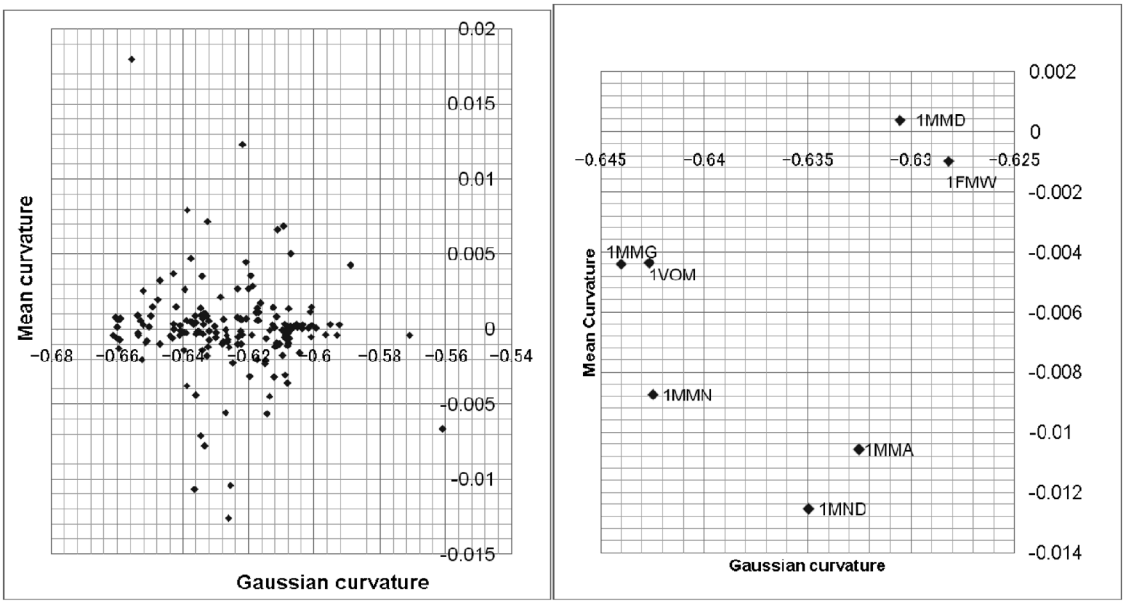


Fig. 3 Gaussian and mean curvatures of the ribose. (A): ATP molecules binding to Pi release proteins. (B): ATP–analog bound to myosin.



(A) (B)

Fig. 4 Gaussian and mean curvatures of the adenine five-membered ring. (A): ATP molecule binding to Pi release proteins. (B): ATP–analog bound to myosin.



(A) (B)

Fig. 5 Gaussian and mean curvatures of the adenine six-membered ring. (A): ATP molecule binding to Pi release proteins. (B): ATP–analog bound to myosin.

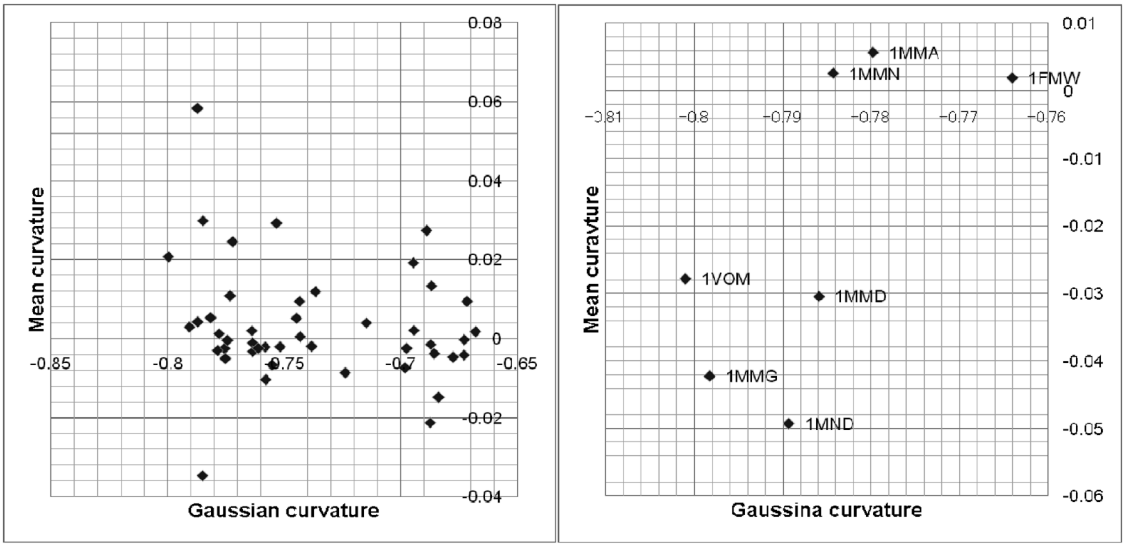


Fig. 6 Gaussian and mean curvatures of the adenine hinge. (A): ATP molecule binding to Pi release proteins. (B): ATP–analog bound to myosin.

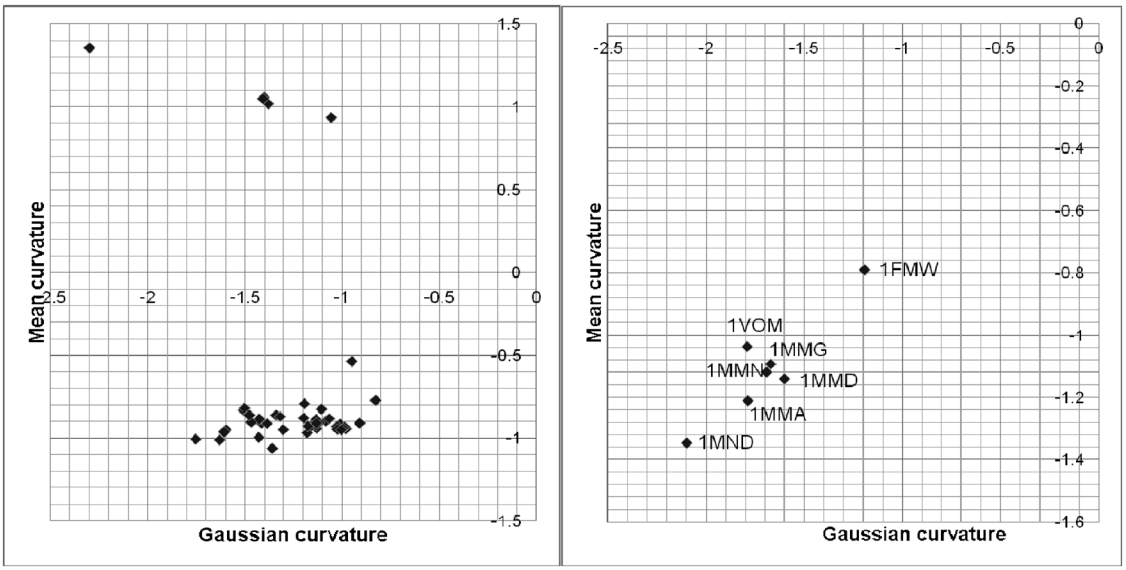


Fig. 7 Gaussian and mean curvatures of the connecting part between the adenine and ribose. (A): ATP molecule binding to Pi release proteins. (B): ATP–analog bound to myosin.

hexagons. The covalent bonds between atoms were not taken into account. The same assignment rule for ordering was applied to hinge curvature calculation. The adenine hinge curvatures are shown in Fig. 6.

We also investigated the relationship between rings in adenine and ribose. To apply ring curvature calculation, we selected the atoms connecting adenine and ribose rings; we calculated the curvature for the set of atoms $\{O_1', C_1', C_2', C_8, N_9, C_4\}$. The rule for atom ordering was the same as the one for adenine hinge calculation. The results are shown Fig. 7. As seen in Fig. 7, the curvature values for the connection between adenine and ribose rings for ATP molecules bound to Pi release proteins are divided into two groups, namely, one with negative mean curvature side and the other with positive mean curvature side. Almost all of the curvature values of ATP molecules bound to Pi release proteins were found in the negative-mean-curvature group and only a few cases were found in the positive-mean-curvature group.

5. Summary

We are aiming to elucidate the mechanisms of ATP hydrolysis from the viewpoint of atomic resolution. We characterize adenine and ribose rings using discrete scheme of surface curvature at the gravity center. The ring conformations of ATP and relationship between rings can be described by Gaussian and mean curvature values. The values of Gaussian and mean curvatures of ATP–analogs bound to myosin were compared with the corresponding curvatures of ATP molecules bound to Pi-release proteins. Thus we obtained the following results,

· Ribose:
The curvature values locate in the area of Pi release ATP.

· Adenine five-membered ring:
The curvature values of 1FMW and 1VOM are in the area of Pi release ATP, but others are not. They go down almost straightly in K–H plane.

· Adenine six-membered ring:
The curvature values of 1FMW, 1MMD, 1MMG, and 1VOM are in the area of Pi-release ATP, while those of 1MMN, 1MMA, and 1MND are at the lower side of the Pi-release area. The latter cases are minor ones of ATP conformation.

· Adenine Hinge:
The curvature distribution of ATP bound to Pi-release protein seems to be divided into two groups, i.e., left-side group and right-side group. The curvature values of 1FMW, 1MMA and 1MMN are on the left side of the group, whereas 1VOM, 1MMD, 1MMG and 1MND are out of the area for the Pi-release ATP.

· Adenine-Ribose:
The curvature value of only 1FMW is in the area of Pi-release ATP area. Other ATP–analogs are out side the area.